U.S. High Production Volume (HPV)
Chemical Challenge Program

SUMMARY OF EXISTING DATA, COMPLETED TEST PLAN AND RATIONALE FOR COBALT BORATE NEODECANOATE COMPLEXES (CASRN 68457-13-6)

Prepared by

MorningStar Consulting, Inc.

On Behalf of the Sponsoring Companies:

The Shepherd Chemical Company and OM Group Americas

DATE: July 12, 2008

TABLE OF CONTENTS

INTRODUCTION 4

USE PATTERNS AND REGULATORY BACKGROUND 4

Bioequivalency 6

Comparative Toxicity and Pharmacokinetics 8

SUPPORTING DATA FOR DISSOCIATION PRODUCTS 10

Neodecanoic Acid 10

Boric Acid 11

Cobalt 11

EXISTING DATA FOR COBALT BORATE NEODECANOATE AND DISSOCIATION PRODUCTS - SUMMARY 12

Physicochemical Properties 12

Environmental Fate and Transport 14

Ecotoxicity 15

Human Health Effects 16

TEST PLAN AND RATIONALE FOR COBALT BORATE NEODECANOATE . 26

Physicochemical Properties 26

Environmental Fate Parameters 26

Ecotoxicity 27

Human Health Effects 27

REFERENCES 30

Tables

Table 1. Results of extraction of cobalt from surrogate biological fluids……7

Table 2. A comparison of acute oral toxicity values of cobalt compounds calculated based on the weight of each compound or on the cobalt content of each respective compound……9

Table 3. Summary of existing data for cobalt borate neodecanoate and its dissociation products……22

Table 4. Test Plan Matrix: Cobalt borate neodecanoate……28

Figures

Figure 1. Structure of neodecanoic acid 4

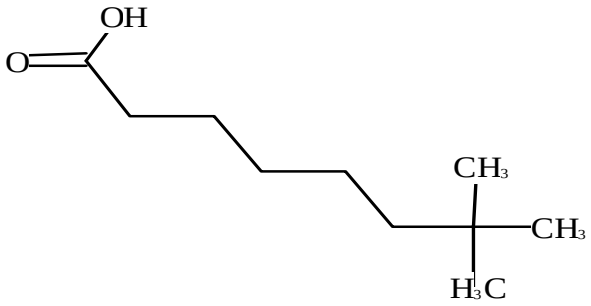
INTRODUCTION

The following document includes a summary of existing data and a completed test plan for cobalt borate neodecanoate complexes [CASRN 68457-13-6]. The information provided in this document and the attached dossier of robust summaries meets the requirements under the U.S. High Production Volume (HPV) Chemical Challenge. Cobalt borate neodecanoate is one of 19 sponsored chemicals organized under the Metal Carboxylates Coalition (The Coalition), an HPV testing consortium managed by the Synthetic Organic Chemical Manufacturers Association's (SOCMA) VISIONS Department. The Coalition member companies sponsoring cobalt borate neodecanoate are The Shepherd Chemical Company and the OM Group (OMG).

USE PATTERNS AND REGULATORY BACKGROUND

Cobalt borate neodecanoate complexes are salts of neodecanoic acid, which is a C-10 carboxylic acid, and thus a member of the metal carboxylates group. Cobalt and boron can associate with neodecanoic acid in a variety of ways and thus, the material is referred to as "complexes." The structure of neodecanoic acid is presented in Figure 1.

Figure 1: Structure of neodecanoic acid



MolWt: 172.27 C10 H20 O2
026896-20-8 Neodecanoic acid

All of the metal carboxylate salts are designed to add metals to chemical reactions. They therefore are expected to dissociate into free metal and free acid.

In general the cobalt carboxylates are used as oxidative polymerization catalysts in many product areas. These areas include but are not limited to: ink and paint driers; unsaturated polyester resins, and hydrodesulfurization in their manufacturing; and the making of the insecticide DEET (diethyltoluamide). Some of these carboxylate compounds are used in oxygen scavenger plastics as well (for example, plastic bottles). The tire industry also uses cobalt carboxylates as adhesion promoters in tire manufacturing. These compounds facilitate adhesion between the rubber in the steel cords. The metal (not salt) loadings range from 0.01-0.5% depending upon the application listed above.

One characteristic of cobalt borate neodecanoate and other metal carboxylates is that they readily dissociate from an ion pair into free metal and free acid. They are found as partially dissociated products in the ambient environment (i.e., neutral pH). Dissociation is a reversible process and the proportion of dissociated salt is dependent on the pH and pKa (the dissociation constant), which is the pH at which 50% dissociation occurs. In the low pH environment of the digestive tract (e.g., pH 1.2) complete dissociation will occur for these metal carboxylates. The transport and bioavailability of the metals and acids are determined by their solubility in environmental media and biological fluids which is determined by environmental parameters such as pH.

Dissociation is a reversible reaction, splitting the parent compound into two or more chemical species which may be ionic, but are not necessarily so. The process can be generally represented as:

$$[RCOO^-]_x{:}[M^+] \overset{pK1}{\leftrightarrow} [RCOO^-]_x + [M^+] \overset{pK2}{\leftrightarrow} [RCOOH]_x + [M^+]$$

undissociated salt — **dissociated acid and metal** — **neutral species + ionized metal**

High pH — Low pH

The pKa and pH are equal when the metal carboxylate salt is 50% dissociated. The parent compounds, the metal carboxylate salts, are associated ionized molecules.

The Metal Carboxylates Coalition conducted a study following OECD Guideline 112 to determine the dissociation constant of cobalt borate neodecanoate. The mean pKa value was 6.41 at 20ºC. This result indicates that a moderate amount of dissociation will occur at approximately neutral pH (i.e., representative of aquatic and marine ecosystems), while complete dissociation will occur at the physiologically relevant pH of the mammalian stomach (pH 1.2). These findings are particularly important in relating available data for neodecanoic acid, cobalt and boron to support the existing data for cobalt borate neodecanoate in the fulfillment of critical endpoints.

Because the free acid (neodecanoic acid) and corresponding free metal (cobalt) and non-metallic element (boron) have different characteristics (e.g., solubility, adsorption, and toxicity) than the undissociated salt (ion pair), the proportion of dissociation influences the behavior of the substance in the environment and *in vivo*. The bioavailable fraction of the constituents of metal carboxylate salts can be estimated from the dissociation constants.

There are two principal hazard assessments being evaluated based on the current data for cobalt borate neodecanoate. The first is the hazard to aquatic organisms due to environmental exposure. The second is hazard to mammalian systems as a result of oral exposure. Based upon the pKa of 6.41, it is expected that in the ambient aquatic environment, moderate portions of the cobalt borate neodecanoate will be dissociated; therefore, part of the compound will be present as neodecanoic acid, boric acid, and cobalt cations. In the environment (i.e., aquatic systems), toxicity is typically related to the free metal ion concentration (U.S. EPA, 2002). The metal ion pair (salt) is less likely to be absorbed and to contribute to toxicity. Boric acid is weak acid with a pKa of 9.2, and thus it exists primarily as the undissociated acid (H_3BO_3) in aqueous solution at environmental pH values (U.S. EPA, 2004). Toxicity data for boric acid is used thus used to estimate the potential hazard of the boron component of cobalt borate neodecanoate to aquatic organisms.

At the low pH of the mammalian stomach (pH 1.2) all of the metal carboxylates, including cobalt borate neodecanoate, are expected to be completely, or nearly completely, dissociated. This indicates that when administered orally, the absorption and resulting toxicity would be due to the independent action of the neodecanoic acid, the free (ionized) cobalt, and boric acid. This is supported by *in vivo* and *in vitro* data with cobalt acetate and other cobalt containing carboxylates (Firriolo 1992.; Speijers et al 1985; Stopford et al. 2003) (See discussion below).

The dissociation constant shows that at the pH of the stomach, the important moieties from a toxicological standpoint are the unionized free neodecanoic acid, ionized cobalt, and boric acid. Because of this dissociation in the stomach, mammalian toxicity data for neodecanoic acid can to serve as a surrogate data for the carboxylic acid component of cobalt borate neodecanoate. Similarly, under these conditions, data for cobalt can be represented by fate and toxicity data for free ion or simple metal salts (e.g., cobalt chloride) and data for boron can be represented by fate and toxicity data for boric acid. Therefore, the role in any observed toxicity for acids and metals can be evaluated independently.

Bioequivalency

The work described below by Stopford et al. (2003) shows that cobalt chloride is similar to, or more bioavailable than, the corresponding cobalt carboxylate salts,

which makes the chloride a conservative surrogate in estimating bioavailability and toxicity of dissociated metal. Cobalt chloride has thus been emphasized during preparation of the attached robust summaries and provides the preferred surrogate data for cobalt carboxylate salts, including cobalt borate neodecanoate.

The recent studies by Stopford et al. to evaluate the "bioequivalency" (an estimate of bioavailability) of cobalt compounds included three cobalt carboxylates and cobalt chloride (when added as fine powders) in synthetic fluids designed as surrogate gastric juices. These investigators showed that these cobalt salts were completely dissociated and dissolved at a gastric pH (1.2) (Table 1). When added to surrogate intestinal fluids at neutral pH (7.4), $Co(II)Cl_2$ was also highly soluble. The solubility of the cobalt (% available cobalt expressed as Co(II) ion) in cobalt carboxylates ranged from 30.8 to 50.8 percent available cobalt at 72 hours (Table 1). These results for cobalt chloride and cobalt naphthenate are highly consistent with data reported by Firriolo (1992) for these same salts in similar surrogate biological fluid matrix (Table 1). Maximum solubility of Co naphthenate was observed at 48 hrs, which was the longest sample time used in the study.

These bioequivalency data are valuable for two reasons. They confirm the prediction from the dissociation studies that these compounds are expected to be completely dissociated in the gastrointestinal tract (low pH) and a substantial proportion of these compounds would be expected to be dissociated and bioavailable in water at neutral pH (7.4).

Table 1: Results of extraction of cobalt from surrogate biological fluids

Matrix (pH)	**Maximum Solubility (% of available metal)**			
	$CoCl_2$	Co 2-ethyl-hexanoate	Co naphthenate	Co neodecanoate
Gastric pH (1.5)[a]	100	100	100	100
Gastric pH (2.0)[b]	100		100	--
Intestinal pH (7.4)[a]	100	50.8*	45.4*	30.8*
Intestinal pH (7.3)[b]	85	--	20**	--

[a] From Stopford et al. (2003); [b] Firriolo (1992)
* Maximum concentration observed at 72 hours.
** Maximum concentration observed at 48 hours.

Stopford et al. (2003) and Firriolo (1992) added all of the salts to the neutral (intestinal) surrogate solutions as finely ground powder. It is not surprising that the percent of available cobalt from cobalt carboxylates appears to increase with time (48 or 72 hours). Firriolo (1992) also evaluated the solubility of ground and ethanol-solubilized cobalt naphthenate in a neutral buffer solution[1]. For ground

[1] PBS = phosphate buffered solution without $CaCl_2$ or $MgCl_2$

cobalt naphthenate, 20% of available Co(II) was dissociated. In contrast, 90% of available cobalt was observed as dissociated Co(II) when originally introduced in ethanol. The ethanol-solubilized Co(II) remained in solution. This finding has implications for dissociated Co(II) introduced to the intestine solubilized in gastric juices.

Cobalt is absorbed primarily as the free Co(II) ion via biochemical mechanisms at the intestinal mucosal wall (Firriolo 1992). Having been reported as completely soluble in gastric fluids (Stopford et al. 2003; Firriolo 1992), Co(II) should remain soluble (100% dissociated Co(II)) after entering the intestine from the stomach. Once solubilized, this cobalt would be expected to undergo the same fate irrespective of the salt originally ingested. Stopford et al. (2003) emphasized the importance of confirming the interpretation of *in vitro* solubilities in surrogate fluids with *in vivo* data. In fact, Firriolo used these (Table 1) *in vitro* solubility tests as preliminary studies for subsequent comparative absorption, distribution and elimination studies. Discussion of *in vivo* data is presented in the following section.

Finally, the work by Stopford et al. (2003) shows that the metal chloride is similar to, or more bioavailable than, the corresponding metal carboxylate salts (Table 1), which makes the chloride a conservative surrogate when attempting to estimate the bioavailability and toxicity of dissociated metal salts. For this reason, data for the chlorides of cobalt have been emphasized during preparation of the attached robust summaries and is the preferred surrogate for the cobalt dissociation product of cobalt borate neodecanoate.

Comparative Toxicity and Pharmacokinetics

Toxicity data for soluble cobalt salts indicate that the contribution of the respective anion to the toxicity of the compound is negligible compared with that of the cobalt cation. Speijers et al. (1982) investigated the acute oral toxicity in rats of a series of cobalt compounds including cobalt acetate. Lethal doses varied significantly when calculated in terms of the compound weight; however, when based on the dose of the Co(II) ion, all of the LD50 values were within a factor of about two for all of the compounds (Table 2). With the exception of the fluoride and bromide salts, all other salts tested had LD50 values within the range from 140 to 190 mg Co/kg bw. The LD50 for cobalt acetate was in the middle of this range at 168 mg Co/kg bw. This work indicates that toxicity is related to the cobalt ion and independent of counter ions. Similar results would be expected for cobalt borate neodecanoate.

Table 2. A comparison of acute oral toxicity values of cobalt compounds calculated based on the weight of each compound or on the cobalt content of each respective compound.

Compound	LD50* (mg compound /kg bw)**	LD50* (mg Co/kg bw)
Cobalt(II) fluoride	150	91
Cobalt(II) oxide	202	159
Cobalt(II) phosphate	387	187
Cobalt(II) bromide	406	109
Cobalt(II) chloride	418	190
Cobalt(II) sulphate	424	161
Cobalt(II) nitrate	434	140
Cobalt(II) acetate	503	168

* Data from Speijers et al. (1982)
** Several test compounds were hydrates and contained water. Results are expressed based on the weight of the anhydrous compound.

This toxicity data is supported by evaluation of the absorption, distribution, and elimination of cobalt following exposure to different metal salts. Work by Firriolo et al. (1999) showed that regardless of whether the compound was introduced as Co(II) chloride or Co naphthenate, the absorption, disposition, and elimination of cobalt was the same. This data indicates that the carboxylic acid portion of the salt does not play a role in cobalt ion absorption *in vivo* once the compound (ion pair) has dissociated. These authors state that absorption of cobalt in the GI tract is dependent upon release of free metal ion and their results indicate that the acid, in this case naphthenate, does not limit the degree of absorption.

Firriolo et al. (1999) confirmed previous findings that cobalt absorption occurs in the jejunum of the small intestine. Working with intestinal rings, these authors showed that absorption of cobalt occurred via biochemical processes that occurred at the intestinal mucosal wall. These processes appear to be saturable and both concentration and temperature dependent (Firriolo, 1992). These characteristics are indicative of active transport (Ashmead et al., 1985 and Firriolo et al., 1999). In addition, there appears to be a diffusional component to the absorption of cobalt ions, which is also concentration dependent (Firriolo et al., 1999). Despite the presence of these mechanisms for cobalt absorption, uptake from the gut is incomplete. Only limited absorption of ingested cobalt occurs (e.g., 20% – 30%) in the gut (Firriolo, 1992; ASTDR, 2001).

The *in vivo* toxicity (Speijers et al., 1982) and absorption/distribution data (Firriolo et al. 1999) are supported by the *in vitro* data for a broader range of cobalt carboxylates (Stopford et al., 2003; Firriolo, 1992; Firriolo et al., 1999). This body of work shows that the hazard of these metal carboxylates is largely dependent on the metal, and not the carboxylic acid. This facilitates the use of toxicity data for soluble metal salts (e.g., $Co(II)Cl_2$) that dissociate rapidly and completely

under physiological conditions, to estimate the potential hazard of cobalt borate neodecanoate.

Supporting Data for Dissociation Products

Consistent with discussions between the Metal Carboxylates Coalition and the EPA, data for the dissociation products (metals and acids) are recognized as being essential to understanding the environmental fate and toxicological characteristics of the respective metal carboxylate salts. Data for neodecanoic acid, cobalt chloride, and boric acid are therefore useful in characterizing the hazard of cobalt borate neodecanoate.

In summary, the key points relative to cobalt borate neodecanoate are:

- Dissociation to neodecanoic acid, boric acid and cobalt (described as cobalt chloride);
- Dissociation constant (pK values) in the circum neutral range;
- Complete or nearly complete dissociation at gastric pH (1.5 to 2.0);
- A moderate amount of dissociation in the environmental pH range (neutral);
- Existing data for the parent molecule or its dissociation products will be sufficient to address specific endpoints.

Data for cobalt boron neodecanoate and its dissociation products are provided as follows:

1. Data for cobalt borate neodecanoate are provided in robust summary format in Appendix A.

2. In addition, when available, data for the dissociation products (neodecanoic acid, boric acid, and cobalt chloride) are provided.

    a. Appendix B contains a synthesis of robust summaries for neodecanoic acid. The IUCLID dataset for neodecanoic acid is attached as Appendix C and robust summaries prepared by ExxonMobil Chemical Company for C5-C-28 neoacids, a category which includes neodecanoic acid, are attached as Appendix D.
    b. Appendix E contains robust summaries for boric acid.
    c. Appendix F contains robust summaries for cobalt chloride.

Neodecanoic Acid

Neodecanoic acid is relatively resistant to biotransformation and does not readily form bioactive metabolites (ExxonMobil Chemical Company, 2002). Thus it would

be primarily eliminated in the urine as glucuronic acid conjugates or by dealkylation (Katz and Guest, 1994).

The robust summaries for neodecanoic acid were largely derived from information in the IUCLID dataset for neodecanoic acid (attached as Appendix C) and in robust summaries prepared by Exxon-Mobil Chemical Company for the Neoacids (C5 – C28) Category, which includes neodecanoic acid (attached as Appendix D). In addition, these data are summarized and referenced in the appropriate remarks sections for each data element in the robust summaries of cobalt borate neodecanoate. Data for neodecanoic acid are discussed in the next section and summarized in Table 3.

Boric Acid

Boron is a non-metallic element with an oxidation state of +3. Boron is naturally-occurring and widespread in nature at relatively low concentrations (Woods, 1994). Concentrations in fresh water range from <0.01 – 1.5 ppm. Boron in the environment is always found chemically bound to oxygen, usually as alkali or alkaline earth borates, or as boric acid (U.S. EPA, 2004).

Boron is well absorbed from the gastrointestinal tract following oral exposure in humans and animals. There is no evidence that boron compounds are metabolized in the body. Administered boron is excreted in a short time in both humans and animals, with clearance primarily through the urine. Boron is absorbed during inhalation exposure but not across intact skin in humans or animals. Studies suggest that boric acid and borate compounds exist in the body primarily as undissociated boric acid, which distributes evenly throughout the soft tissues of the body, but shows some accumulation in bone (U.S. EPA, 2004).

The robust summaries for boric acid were derived largely from the well recognized and peer reviewed document *Toxicological Review of Boron and Compounds* (U.S. EPA, 2004). These robust summaries are presented in Appendix E. In addition, these data are summarized and referenced in the appropriate remarks sections for each data element in the robust summaries of cobalt borate neodecanoate. Data for boric acid are discussed in the next section and summarized in Table 3.

Cobalt

Cobalt is a naturally-occurring element that has properties similar to those of iron and nickel. It is an essential element, required for good health in animals and humans (ASTDR, 2001). A biochemically important compound containing cobalt is vitamin B_{12} or cyanocobalamin. For most people, food is the largest source of cobalt intake. The average person consumes about 11 micrograms of cobalt per day in their diet (ASTDR, 2001). Part of this cobalt comes from vitamin $B_{12,}$ which is found in meat and dairy products. Cobalt is also found in surface and

groundwater. In the U.S., concentrations in water are usually between 1 and 10 µg/L (ppb), although they may be much higher in areas that are rich in cobalt-containing minerals or in areas near mining or smelting operations. In most drinking water, cobalt levels are less than 1 – 2 ppb (ASTDR, 2001).

Soluble forms of cobalt, such as cobalt(II) chloride (or cobaltous chloride), are most likely to be absorbed and cause systemic effects in humans. For this reason, this compound has often been used in absorption and toxicology studies to determine the potential hazard of cobalt exposures. When coming into contact with water and biological fluids, cobaltous chloride dissolves and releases cobalt as a +2 ion. In general, it is the cobalt ion that is responsible for causing toxicity[2]. Because of this, in this document, the toxicity of cobalt(II) chloride (expressed in terms of the cobalt ion), is used as a surrogate for the toxicity of cobalt that is released through the dissociation of the cobalt borate neodecanoate.

Approximately 13-34% of cobalt(II) chloride is absorbed in the gut of rats. Absorption may be increased in iron deficient individuals. The highest concentration of absorbed cobalt is in the liver and then the kidney. There is no accumulation of cobalt with age. Following oral exposure, cobalt is eliminated primarily in feces (the unabsorbed fraction) and secondarily in urine (the absorbed fraction). For cobalt(II) chloride, 70 - 80% of the administered dose is eliminated in the feces. Elimination is biphasic or triphasic. The terminal phase involves a very small residual level of cobalt and has a half-life in years (ATSDR, 2001).

The robust summaries for cobalt chloride were derived largely from well recognized and peer reviewed compendia (e.g., ATSDR Toxicological Profiles, WHO Environmental Health Criteria). These data are presented in Appendix F. In addition, these data are summarized and referenced in the appropriate remarks sections for each data element in the robust summaries of cobalt borate neodecanoate. Data for the soluble/dissociable forms of the metal (free metal or the chloride salt) are discussed in the next section and summarized in Table 3.

EXISTING DATA FOR COBALT BORATE NEODECANOATE AND DISSOCIATION PRODUCTS - SUMMARY

Physicochemical Properties

[2] Insoluble compounds that do not release significant amounts of the cobalt ion are much less toxic when administered orally (ASTDR, 2001). The oral toxicity of soluble cobalt compounds is similar when expressed in terms of the cobalt ion.

Available physicochemical property data for cobalt borate neodecanoate, and for neodecanoic acid, boric acid, and cobalt chloride, are shown in Table 3 and briefly summarized below. The sources of information for these data are given in the robust summaries (Appendixes A – F).

Recent studies were conducted to determine the melting point, boiling point, and water solubility for cobalt borate neodecanoate. Data for all relevant physico-chemical endpoints are available for neodecanoic acid, boric acid, and cobalt chloride (Table 3).

Melting Point

A GLP study was conducted according to OECD Guideline 102, using the capillary method, to determine the melting point/melting range of cobalt borate neodecanoate. No clear melting point could be observed. Above approximately 103ºC, degradation occurred and gaseous degradation products were formed. For neodecanoic acid, the melting point was reported as 57.13^{o}C; for boric acid, 169ºC; and for cobalt chloride, 735ºC.

Boiling Point

A GLP study was conducted according to OECD Guideline 103, using the capillary test, to determine the boiling point/boiling range of cobalt borate neodecanoate. The test substance did not boil under atmospheric pressure, and gaseous degradation products were formed above approximately 125ºC. For neodecanoic acid, the boiling point was reported as 243-253^{o}C; for boric acid, 300ºC (a temperature at which half the water was lost); and for cobalt chloride, the reported boiling point was 1,049ºC.

Density

The density for cobalt borate neodecanoate is reported as 1.32 g/cm^3 at 25ºC; as 0.91 g/m^3 at 20ºC for neodecanoic acid; as 1.435 g/cm^3 at 15ºC for boric acid, and as 3.367 g/cm^3 at 25ºC for cobalt chloride.

Vapor Pressure

Vapor pressure was not considered applicable for boric acid or cobalt chloride. The reported vapor pressure for neodecanoic acid was 0.29 hPa at 50^{o}C.

Partition Coefficient

The octanol/water partition coefficient is not applicable for inorganic chemicals such as boric acid and cobalt chloride. The log octanol/water partition coefficient for neodecanoic acid was reported to be 3.90.

Water Solubility

A GLP study was conducted, following OECD Guideline 105, using the column elution method, to determine the water solubility of cobalt borate neodecanoate. The water solubility was estimated to be 51.2 mg/L at 20ºC. The water solubility of neodecanoic acid is similar, reported to be 68.97 mg/L at 25ºC. Boric acid and cobalt chloride are an order of magnitude more soluble in water, with reported values of 63.5 g/L at 30^{o}C and 450 g/L at 7^{o}C, respectively.

Environmental Fate and Transport

Available environmental fate and transport data for cobalt borate neodecanoate, and for neodecanoic acid, boric acid and cobalt chloride are shown in Table 3 and briefly summarized below. The sources of information for these data are given in the robust summaries (Appendices A – F).

Data exist for dissociation in water for cobalt borate neodecanoate, but not for any other fate characteristics. Relevant information for the dissociation products is discussed below.

Photolysis

Neodecanoic acid is predicted to undergo indirect photolysis with a half-life of 17 hours, according to AOP v.1.91 in the EPIWIN v.311 program. The photodegradability of boric acid and cobalt chloride is not relevant, as the elements boron and cobalt do not degrade further.

Dissociation in water

One key characteristic of any metal carboxylate is that it readily dissociates from an ion pair into free metal and free acid as the pH is decreased. A dissociation study was conducted according to OECD 112, under GLPs, to determine the equilibrium constant of cobalt borate neodecanoate. The results indicate the pKa was 6.41 at 20ºC (Lezotte and Nixon, 2002). The reported pKa for boric acid is 9.2 (U.S. EPA, 2004).

Biodegradation

In a recent GLP study Co B neodecanoate was “not readily biodegradable” with 4,45% degraded during a 28 days. The study was conducted according to OECD method 301B (McLaughlin 2007). In an earlier study conducted. according to a manometric respirometry test (OECD 301F), neodecanoic acid is not readily biodegradable, with only 11% degradation after 28 days. Biodegradation is not relevant for the elements boron and cobalt. New data shows a similar level of biodegradation metal carboxylate.

Monitoring data

No monitoring data were reported.

Transport data

Estimation of environmental transport for cobalt borate neodecanoate is not available since fate models generally used do not accurately predict salts such as metal carboxylates. However, the distribution of neodecanoic acid was predicted using the Level III Fugacity model in EPIWIN v.3.11. Assuming equal input to all compartments, the distribution was predicted as 3.55% in air, 37% in water, 57.5% in soil and 1.96% in sediment.

Ecotoxicity

Available ecotoxicity data for cobalt borate neodecanoate, neodecanoic acid, boric acid, and cobalt chloride are shown in Table 3 and briefly summarized below. The sources of information for these data are given in the robust summaries (Appendixes A – F).

Fish Toxicity

A GLP study was conducted according to OECD Guideline #201 as part of the recent testing program. And the results are shown in Table 3 expressed as Co B Neodecanoate and as Co(II) ion (Sayers 2008).

Neodecanoic acid
Static acute renewal tests of water-accommodated fractions of neodecanoic acid indicated a 96-h LC50 for rainbow trout (*Oncorhynchus mykiss*) of 37.2 mg/L; other reported values range from 32 – 181 mg/L.

Boric acid
When tested on two stages of the fry of chinook salmon (*Oncorhynchus tshawystcha*) and coho salmon (*Oncorhynchus kisutch*), the 96-h LC50 of boric acid ranged from 78.2 – 127 mg B/L. Other reported 96-h LC50 values for boron in fish range from 14.2 mg B/L in zebrafish to 978 mg B/L in mosquito fish.

Cobalt chloride
For cobalt chloride, the 96-h LC50 was 1.41 mg Co/L for the highly sensitive rainbow trout, *Oncorhynchus mykiss*. Other fish species were less sensitive with 96-h LC50 values ranging from 22.0 to 330 mg Co/L.

Invertebrate toxicity

A GLP study was conducted according to OECD Guideline #202 as part of the recent testing program. And the results are shown in Table 3 expressed as Co B Neodecanoate and as Co(II) ion.

Neodecanoic acid
For neodecanoic acid, the 48-h LL50 (lethal limit for 50%) to *Daphnia magna* was reported as 47.1 mg/L, while the 96-h LC50 for the copepod *Acartia tonsa* was 25 mg/L.

Boric acid
For boric acid, reported 48-h EC50 values for *Daphnia magna* include 133 mg B/L and 226 mg B/L.

Cobalt chloride
For cobalt chloride, reported 48-h EC50 values for *Daphnia magna* include 1.52 mg Co/L and 5.5 mg Co/L. For *Ceriodaphnia dubia*, 48-h LC50 values ranged from 2.35 to 4.60 mg Co/L.

Algal toxicity

A GLP study was conducted according to OECD Guideline #203 as part of the recent testing program. And the results are shown in Table 3 for growth and yield expressed as Co B Neodecanoate and as Co(II) ion for each endpoint (Hoberg 2007).

Boric acid
For boric acid, a 14-day exposure of *Chlorella pyrenoidosa* resulted in a NOEC of 0.4 mg B/L and a LOEC of 0.8 mg B/L. The 72-h EC50 for boric acid for *Scenedesmus subspicatus* was 34 mg B/L and the 96-h EC50 for the duckweed *Lemna gibba* was > 60 mg/L.

Cobalt chloride
For cobalt chloride, the 96-h EC50 for *Chlorella vulgaris* was 0.52 mg Co/L. For the duckweed *Lemna minor*, the 7-d IC50 was 16.9 mg Co/L, while for the blue-green alga *Spirulina platensis*, the 96-h EC50 was 23.8 mg Co/L.

There are no ecotoxicity data on cobalt borate neodecanoate. Neodecanoic acid is moderately toxic to fish and invertebrates; toxicity to algae is unknown. Boric acid and cobalt chloride are of moderate to low toxicity to fish and invertebrates, but appear to be highly toxic to at least some species of aquatic plants

Human Health Effects

There were no data available on the mammalian toxicity of cobalt borate neodecanoate, but three new mammalian studies have been conducted. However, the majority of the human health effects endpoints are satisfied for the dissociation products, neodecanoic acid, boric acid, and cobalt chloride. These data are shown in Table 3 and briefly summarized below. The sources of information for these data are given in the robust summaries (Appendixes A – F).

Acute Mammalian Toxicity

As part of a recent testing program, the LD50 was estimated using OECD Guidleine #425, the up and down method. The study was conducted under GLP and results are presented in Table 3 (Finlay 2007).

Neodecanoic acid

Acute toxicity data are available for neodecanoic acid for five of five acute endpoints (i.e., oral toxicity, inhalation toxicity, dermal toxicity, skin irritation and eye irritation) as presented in Table 3. Neodecanoic acid shows a low order of acute toxicity. Oral, inhalation and dermal LD50 or LC50 values are 2000 mg/kg (rat), >511 mg/m^3 (6 hrs., rat), and >3160 mg/kg (rabbit) or >3640 mg/kg (rat), respectively. Neodecanoic acid was non-irritating to the skin when tested on the rabbit according to OECD Guideline 404, but did cause eye irritation in the rabbit using the Draize test.

Boric acid

The oral LD50 for boric acid was 550 – 710 mg B/kg in rats and 603 mg B/kg in mice. No toxic effects were seen from an inhalation exposure of mice to amorphous elemental boron, a form of boron is not relevant to this assessment. Boric acid was found to be a mild to moderate irritant to the skin of rabbits and guinea pigs.

Cobalt chloride

There are extensive toxicity data available for cobalt (II) chloride and several other soluble and insoluble salts of cobalt. The single-dose rat LD50s for cobalt (II) chloride range from 42.4 to 190 mg Co/kg bw. For the mouse, the LD50 value expressed as the cobalt ion is 89.3 mg Co/kg bw. Inhalation toxicity data are not available for cobalt chloride. Increased proliferation of lymphatic cells was seen in rats, mice, and guinea pigs dermally exposed to cobalt chloride in DMSO once per day for 3 consecutive days, with LOAEL values ranging from 9.6 to 14.7 mg Co/kg-day. Dermatitis, probably caused by an allergic reaction, is a common result of dermal exposure to cobalt in humans.

Repeated Dose Toxicity

See OECD 422 data under Reproduction, below.

Neodecanoic acid

Repeated dose studies have been conducted on neodecanoic acid for several species and several exposure routes. When administered to rats in their feed for 3 months, the NOAEL for a 30% preparation of neodecanoic acid was 500 ppm. The LOAEL was 1500 ppm and included changes in the renal tubules of both male and female rats. Morphological changes in the thyroid, including hyperplasia, were also seen in male rats at the 1500 ppm level. Beagle dogs

receiving oral capsules containing neodecanoic acid daily for a period of 13 weeks did not show adverse effects at 30 mg/kg and below, while effects on body weight, hematocrit, hemoglobin and erythrocytes were seen at doses of 94.8 mg/kg and higher. Albino rabbits receiving 10 dermal applications of neodecanoic acid over a 14-day period showed no systemic effects, resulting in a NOAEL of 2.26 g/kg.

Boric acid

Repeated dose studies have been conducted on boric acid with mice, rats and dogs. In a 13-16 week feeding study of boric acid to mice, the NOAEL was at or below 34 mg B/kg-day for males and 47 mg/kg-day for females; the LOAEL was 34 mg B/kg-day. This was based upon the observation of minimal to mild extramedullary hematopoiesis of the spleen in all dosed groups. A 90-day feeding study with rats found testicular atrophy at doses of 26.3 mg B/kg-day and above, identifying this value as the LOAEL and 8.8 mg B/kg-day as the NOAEL for systemic toxicity in rats. In 90-day dietary exposures in beagle dogs, the NOAEL was identified as 3.9 mg B/kg-day for males and 2.5 mg B/kg-day for females.

Cobalt chloride

Oral dosing of rats with cobalt chloride five days per week for 150 to 210 days indicated a LOAEL of 4 mg Co/kg based upon increased organ weights. This is consistent with other studies of cobalt chloride at levels ranging from 0.5 to 30.2 mg Co/kg-day. Repeated oral dosing of rats with cobalt chloride hexahydrate for 8 weeks indicated the NOAEL was 0.6 mg Co/kg and the LOAEL was 2.5 mg Co/kg, based upon changes in hemoglobin content and numbers of erythrocytes. Another study reported oral doses of 0.5 and 2.5 mg Co/kg for 7 months stimulated hematopoiesis and decreased immunological reactivity in rats, while doses of 0.05 mg Co/kg had no effects.

Genetic Toxicity – in vitro

An *in vitro* study was conducted with Chinese hamster ovary cells according to OECD Guideline # 473 (Glatt 2007). Results are shown in Table 3. Under the conditions of the study Co B neodecanoate was found to induce structural chromosome aberrations in mammalian cells with and without activation. The NOAEL for structural chromosome aberrations was 50 ug/ml for 4-h activated and non-activated and were reported as 10 ug/ml for the 20-h non-activated test. Cytotoxic effects were observed at $\geq$ 25 ug/ml and $\geq$ 50 ug/ml during the 20-h and 4-h activated and non-activated studies, respectively. Numerical aberrations were not observed at any dose level or time interval.

Neodecanoic acid

Neodecanoic acid produced negative results in the Ames *Salmonella* assay (OECD Method 471) against four strains of bacteria (e.g., TA 98, TA100, TA1535, and TA1537) when tested with and without metabolic activation.

Neodecanoic acid also produced negative results in a cytogenetic assay (OECD Method 473) with cultured human lymphocytes when tested both with and without metabolic activation.

Boric acid

Results of most short-term mutagenicity studies indicate that boron is not genotoxic. In two different studies, encompassing a total of four bacterial strains, boric acid was negative for mutagenicity in the *Salmonella* assay in both the presence and absence of metabolic activation. In the streptomycin-dependent *E. coli* Sd-4 assay, boric acid was either not mutagenic or produced equivocal results. An isolated positive result for induction of β-galactosidase synthesis was found in *E. coli* PQ37 using the SOS chromotest. Chromosomal aberrations and sister chromatid exchanges did not occur in Chinese hamster ovary cells exposed to boric acid, either with or without activation, and negative results were obtained in mouse lymphoma cell cultures (with and without activation) as well.

Cobalt chloride

Cobalt compounds with a valence state of II, the form of cobalt released by dissociation of cobalt chloride, are generally non-mutagenic in bacterial assays, including plate incorporation and fluctuation assays with *Salmonella typhimurium* TA strains and *Escherichia coli* WP2. However, a weak positive mutagenic response has been found in the rec assay with *Bacillus subtilis* and in Chinese hamster V9 cells. DNA damage in isolated human lymphocytes was observed at 6.0 mg Co/L in the alkaline comet assay, and an increase in sister chromatid exchanges has been observed in human lymphocytes and macrophages.

Genetic Toxicity – in vivo

Neodecanoic acid

There are no *in vivo* genetic toxicity data for neodecanoic acid.

Boric acid

In the mouse micronucleus test, boric acid did not induce chromosomal or mitotic spindle abnormalities in bone marrow erythrocytes.

Cobalt chloride

Oral administration of cobalt chloride hexahydrate to mice (20 – 80 mg/kg bw) produced a concentration-dependent increase in chromosomal aberrations. A dose-dependent increase in the incidence of micronucleated polychromatic erthythrocytes was observed in mice subsequent to i.p. Injection of $CoCl_2.6H_20$, at doses of 25 – 90 mg Co/kg bw. Increased micronucleus formation was observed following i.p. injection of 12.4 and 22.3 mg Co/kg (as cobalt chloride), but not after injection of 6.19 mg Co/kg (NOEL).

In summary, neodecanoic acid and boric acid do not appear to be genotoxic, while cobalt chloride has demonstrated positive effects in various *in vitro* or *in vivo* studies.

Developmental Studies

See Reproduction below.

Neodecanoic acid
No developmental studies with neodecanoic acid are available.

Boric acid
The developmental effects of boric acid have been extensively studied, with studies conducted under the U.S. National Toxicology Program (NTP) using rats, mice and rabbits. All of these studies are rated as "Reliable without Restriction." Dietary exposure in rats from gestation day 6-15 identified a NOAEL of 9.6 mg B/kg-day and a LOAEL of 13.3 mg B/kg-day based upon reduced body weight and skeletal malformations/variations in offspring, as observed at 20 days of gestation. When this study was continued to postnatal day 21, these effects were less severe, resulting in a NOAEL of 12.9 mg B/kg-day and a LOAEL of 25.3 mg B/kg-day, respectively. In another developmental toxicity study with rats exposed to boric acid in the diet, a LOAEL of 13.6 mg B/kg-day was identified based upon fetal body weight. Mice exposed to boric acid in the diet from gestation day 0 – 17 produced offspring with malformations and variations, with a NOAEL of 43.4 mg B/kg-day. Mortality and malformations were observed in rabbits exposed to boric acid from gestation day 6 – 19, with a NOAEL of 21.9 mg B/kg-day and LOAEL of 43.7 mg B/kg-day.

Cobalt chloride
In a developmental toxicity study with cobalt chloride exposure (5.4 to 21.8 mg Co/kg/day) in rats from gestation day 14 to lactation day 21, the LOAEL was based on stunted pup growth. However, maternal toxicity was observed in conjunction with effects on the offspring. This growth effect was considered to be a secondary or indirect effect rather than a direct effect of cobalt on the fetus. No teratogenic effects were observed. Another study in rats provided a NOAEL of 24.8 mg Co/kg/day for cobalt chloride exposure from gestation days 6-15. No effects were observed on fetal growth or survival in mice exposed to 81.7 mg Co/kg/day as cobalt chloride during gestation days 8-12.

Reproduction Studies

A Combined Repeated Dose Toxicity Study with Reproductive/Developmental Screening Test in Rats (OECD Guideline #422) was conducted under GLP as a part of the recent testing program. The only compound related effect was an increase in the sex ratios at the highest dose level of 5.0 ug/ml. The NOAEL is 5.0 ug/ml, the highest level tested in this study (Lewis 2007).

Neodecanoic acid

In an oral (feeding) multi-generation rat reproduction study with neodecanoic acid, no adverse effects were observed in the parental generation or the F_1 and F_2 generations at feeding levels up to 1500 ppm in the diet.

Boric acid

In a study conducted under the U.S. National Toxicology Program, the reproductive toxicity of boric acid was studied in mice using a continuous breeding protocol. The lowest dose, 1000 ppm, decreased sperm motility in F_0 males, marginally decreased epididymal sperm concentration in F_1 males, increased uterine and kidney/adrenal weights and shortened estrous cycles in F_1 females, and reduced litter-adjusted birth weights in F_2 pups, Thus, the LOAEL was 1000 ppm (26.6 mg B/kg-day for males and 31.8 mg B/kg-day for females). In a multi-generation study with rats, a NOAEL of 17.5 mg B/kg-day and LOAEL of 58.5 mg B/kg-day were identified based upon sterility of males and decreased ovulation in females.

Cobalt chloride

Cobalt exposure (as cobalt chloride hexahydrate in drinking water for 12 -13 weeks) affected male reproductive parameters for mice in a time- and dose-dependent manner. All dose levels (23.0 – 72.1 mg Co/kg-day) caused decreases in testicular weight and epididymal sperm concentration. Testicular degeneration and atrophy have been reported in rats exposed to 13.2 to 30.2 mg Co/kg/day as cobalt chloride for 2-3 months in the diet or drinking water.

Other Information

Boric acid

The U.S. National Toxicology Program concluded from a 2-year dietary study in mice that boric acid produced no evidence of carcinogenicity, although the low number of surviving males may have reduced the sensitivity of the study. Based upon a 2-year dietary study in rats, the NTP concluded that there were adequate data to conclude that boric acid was not carcinogenic in rats.

Cobalt chloride

The U.S. National Toxicology Program does not recognize cobalt as a human carcinogen, but IARC has classified cobalt and cobalt compounds as possibly carcinogenic to humans (Class 2B) based on sufficient evidence that cobalt metal powder and cobaltous oxide are carcinogenic in animals. “No studies

were located regarding carcinogenic effects in animals after oral exposure to stable [non-radioactive] cobalt." (ATSDR Sept 2001 Draft).

Table 3. Summary of existing data for cobalt borate neodecanoate and its dissociation products[1]

SIDS ENDPOINT	REPORTED VALUES			
	Cobalt borate neodecanoate	**Neodecanoic acid**	**Boric acid**	**Cobalt chloride**
Physicochemical Properties				
Melting Point	Could not be determined	57.13ºC	169ºC	735ºC
Boiling Point	Could not be determined	243-253ºC	300ºC (looses 1/2 water)	1,049ºC
Density	1.32 at 25ºC	0.91 at 20ºC	1.435 at 15ºC	3.367 at 25ºC
Vapor pressure	NR[2]	0.29 hPa at 50ºC	NR	NR
Log Partition Coefficient	--	3.90	NR	NR
Water Solubility	51.2 mg/L at 20ºC	68.97 mg/L at 25ºC	63.5 g/L at 30ºC	450 g/L at 7ºC
Environmental Fate				
Photodegradation	--	Half life of 17 h for indirect photolysis	NR	NR
Dissociation in water	pKa = 6.41 at 20ºC	--	pKa = 9.2	--
Monitoring Data	--	--	--	--
Transport (Fugacity)	--	3.55% in air, 37% in water, 57.5% in soil, 1.96% in sediment	NR	NR
Biodegradation	4.5% degradation after 28 days --	11% degradation after 28 days	NR	NR
Ecotoxicity				
Fish toxicity (96-h)	4.9 mg/L (rainbow trout) (1.1 mg Co/L) --	37.2 mg/L (rainbow trout)	78.2 – 127 mg/L for salmonid fry	1.41 - 333 mg/L; rainbow trout most sensitive
Invertebrate toxicity (48-h)	9.2 mg/L *Daphnia magna* (2.6 mg Co/L)--	47.1 mg/L (*Daphnia magna*, EC50)	133 – 226 mg B/L (*Daphnia magna*)	1.52 – 5.5 mg Co/L (*Daphnia magna*)
Algae toxicity (72-h)	Growth: EC50 is 0.56 mg/L (0.12 mg	--	0.4 mg B/L (*Chlorella pyrenoidosa*, 14-d	0.52 mg Co/L (*Chlorella vulgaris*, 96-h EC50)

SIDS ENDPOINT	REPORTED VALUES			
	Cobalt borate neodecanoate	**Neodecanoic acid**	**Boric acid**	**Cobalt chloride**
	Co/L) Yield : EC50 0.41 mg/L (0.09 mg Co/L) Pseudokirchneriella subcapitata--		NOEC)	
Human Health Effects				
Acute Oral LD50	Rat LD50 is 1098 mg/kg	2000 mg/kg (rat)	550-710 mg B/kg (rat); 603 mg B/kg (mice)	19.8 – 190 mg Co/kg (rat); 89.3 mg Co/kg (mouse)
Inhalation LC50	--	>511 mg/m^3 (rat, 6-h exposure)	No toxic effects of amorphous elemental boron	--
Dermal LD50		>3160 mg/kg (rabbit); >3640 mg/kg (rat)	--	Increased proliferation of lymphatic cells at 9.6 – 14.7 mg Co/kg-day (various spp.)
Skin irritation		Non-irritating (rabbit)	Mild to moderately irritating (rabbit and guinea pig)	Allergic dermatitis seen in humans
Eye irritation	--	Irritating (rabbit)	--	--
Repeated dose	See Reproduction	500 ppm NOAEL for 3 month oral exposure of rats; 30 mg/kg NOAEL for 13 week oral exposure in dogs; 2.26 g/kg NOAEL for 14 day dermal exposure of rabbits	NOAEL ≤34 mg B/kg-day for male mice and 47 mg B/kg-day for females; NOAEL 8.8 mg B/kg-day for rats; NOAEL 2.5 mg B/kg-day for male dogs and 2.5 mg B/kg-day for females	4 mg Co/kg LOAEL for rats (organ weight changes); 0.6 mg Co/kg NOAEL for rats (blood parameter changes); LOAELs 0.5 – 30.2 mg Co/kg-day for rats in various studies
Genetic toxicity *(in vitro)*	-- Chinese hamster	Negative for	Generally not	Co(2+) generally non-

SIDS ENDPOINT	REPORTED VALUES			
	Cobalt borate neodecanoate	**Neodecanoic acid**	**Boric acid**	**Cobalt chloride**
	ovary cells: N NOAELs of 50 ug/ml for 4-h activated and non-activated and 10 ug/ml for 20-h non-activated.	*Salmonella,* human lymphocytes	mutagenic. Negative for *Salmonella*, Chinese hamster ovary cells and mouse lymphoma cells	mutagenic in most bacterial assays; weak positive response with Chinese hamster V9 cells; DNA damage in human lymphocytes
Genetic toxicity *(in vivo)*	--	--	Negative in mouse micronucleus test	Clastogenic effects in mice
Developmental	See Reproduction--	--	NOAEL = 9.6 mg B/kg/day in rats, 43.4 mg B/kg/day in mice, 21.9 mg B/kg/day in rabbits	NOAEL = 24.8 mg/kg/day in rats; 81.7 mg Co/kg in screening study (mice)
Reproductive	NOAEL is 5.0 mg/kg/day for systemic and reproductive toxcity--	No effects in parental, F_1 or F_2 generations of rats at dietary levels up to 1500 ppm	LOAEL = 26.6 mg B/kg/day for males and 31.8 mg/kg-day for female mice; NOAEL = 17.5 mg B/kg/day in rats	Effects in rats at 13.2 – 30.2 mg Co/kg/day; in mice at 23 – 58.9 mg Co/kg/day

[1] References are given in the robust summaries (Appendixes A – F)
[2] NR = not relevant

TEST PLAN AND RATIONALE FOR COBALT BORATE NEODECANOATE

Cobalt Borate Neodecanoate	CASRN 68457-13-6

The Test Plan for Cobalt borate neodecanoate is presented in Table 4 with supporting data for the dissociation products. The rationale for the Test Plan is based upon existing data as summarized in the previous section and in Table 3.

Physicochemical Properties

Data is available for all five SIDS endpoints listed in Tables 3 and 4 for either the cobalt borate neodecanoate salt or neodecanoic acid, if not both. Although GLP studies were conducted to determine melting point and boiling point of cobalt borate neodecanoate, these endpoints could not be determined under the test conditions. Water solubility for cobalt borate neodecanoate is very similar to that of neodecanoic acid. The vapor pressure endpoint is considered not applicable for the salt. The rationale for not conducting an octanol/water partition coefficient study with cobalt borate neodecanoate is based on the impurity of the compound (i.e. a salt), and an ionizable substance. Using a compound with these characteristics to measure the partition coefficient is inappropriate as it would yield erroneous data. Data are available for neodecanoic acid, which show the Log Kow to be 3.90.

- No additional testing was recommended or proposed for any of the physico-chemical properties.

Environmental Fate Parameters

A GLP study was conducted to determine the dissociation constant for cobalt borate neodecanoate. This is a key property, because the fate and effects of the compound are based upon the dissociation products. Of these dissociation products, environmental fate endpoints such as photodegradation or biodegradation are not relevant for boric acid or cobalt chloride because they are simple compounds that release the elements boron and cobalt which do not degrade further. For neodecanoic acid, experimental data are available for the biodegradation endpoint, based upon a GLP study conducted according to OECD 301F, which indicated that this material is not readily biodegradable. The values for the photodegradation and transport endpoints were predicted using EPIWIN for neodecanoic acid Standard models used for estimating transport do not accurately predict salts or ionized substances and were not used for cobalt borate neodecanoate.

Recommended testing to determine biodegradation has been completed with the following results: Co B neodecanoate was not readily biodegradable according to OECD Guideline 301B. After 28 days the percent ultimate biodegradation, for Co B neodecanoate, procedural control, and toxicity control were calculated to be 4.45, 91.98 and 46.85%, respectively.

Ecotoxicity

Three ecotoxicology studies have been completed with the following results: The trout 96h LC50 is 4.9 mg/L; *Daphnia* 48h EC50 was determined to be 9.2 mg/L; and the algae (*Pseudokirchneriella subcapitata)* 72h EC50s for growth and yield were 0.56 and mg/L, respectively...

Human Health Effects

Acute toxicity studies

An acute oral LD50 study with the rat was conducted for cobalt borate neodecanoate. This study was completed with the following results: The oral LD50 in rats was determined to be 1098 mg/kg using OECD Guideline # 425. Acute toxicity is also well-characterized for the dissociation products for the majority of five endpoints (oral toxicity, inhalation, dermal toxicity, skin irritation, and eye irritation).

Genotoxicity studies

An *in vitro* study with Chinese hamster ovary cells (OECD 473) was conducted with the following results: Under the conditions of this study, cobalt borate neodecanoate was found to induce structural chromosome aberrations in the in vitro mammalian chromosome aberration test in both the non-activated and S9 activated test systems. It was not found to induce numerical chromosome aberrations in any test condition. It was concluded that the test substance was positive in this *in vitro* test the dissociation product neodecanoic acid has been shown to be non-mutagenic *in vitro* in bacteria and human lymphocytes. The genotoxicity of boric acid and cobalt chloride have been well-characterized, with boron showing negative results in a variety of systems and cobalt showing some positive responses. Use of the *in vitro* study with mammalian cell line makes the *in vivo* study unnecessary.

.

Higher tiered studies

A number of repeated dose studies have been conducted with neodecanoic acid, boric acid, and cobalt chloride in a variety of species

The developmental and reproductive toxicity of boron have been extensively investigated with a number of species in U.S. National Toxicology Program studies. Developmental and reproductive toxicity are also well-characterized for cobalt chloride. No effects were seen on reproductive parameters in a multi-generation study with rats on neodecanoic acid.

A combined repeated dose with repro/developmental screen (OECD 422) was completed for cobalt borate neodecanoate with the following results: The study followed OECD guideline 422. The results show that only one compound related effect was observed. In the high-dose level of 5.0 mg/kg/day the sex ratio of F1 litters was increased and appeared to be a compound related effect. All other endpoints and dose levels showed no compound related effects. The NOAEL is determined to be 5.0 mg/kg/day the highest dose level tested in this study.

Based on existing data and the results of studies generated under this test plan no additional studies are required. The test plan as shown in table 4 has been completed.

Table 4. Test Plan Matrix: Cobalt borate neodecanoate

Data elements	Cobalt borate neodecanoate			Neodecanoic acid			Boric acid			Cobalt chloride			Additional Testing recommended for cobalt borate neodecanoate
	Information available	GLP study	Acceptable	Information available	GLP study	Acceptable	Information available	GLP study	Acceptable	Information available	GLP study	Acceptable	
PHYSICOCHEMICAL PROPERTIES													
Melting Point	Y	Y	Y	Y	N	Y	Y	N	Y	Y	N	Y	N
Boiling Point	Y	Y	Y	Y	U	Y	Y	N	Y	Y	N	Y	N
Vapor pressure	N			Y	N	Y	--			--			N
Partition Coefficient	--			Y	N	Y	--			--			N
Water Solubility	Y	Y	Y	Y	N	Y	Y	N	Y	Y	N	Y	N
ENVIRONMENTAL FATE PARAMETERS													
Photodegradation	N			Y	N	Y	--			--			N
Dissociation in water	Y	Y	Y	N			Y	N	Y				N
Transport	--			Y	N	Y	--			--			N
Biodegradation	*Y*	*Y*	*Y*	Y	Y	Y	--			--			*N*
ECOTOXICITY													
Fish toxicity (96-h)	*Y*	*Y*	*Y*	Y	Y	Y	Y	N	Y	Y	N	Y	*N*
Invertebrate toxicity (48-h)	*Y*	*Y*	*Y*	Y	N	Y	Y	N	Y	Y	N	Y	*N*
Algae toxicity (72-h)	*Y*	*Y*	*Y*	N			Y	N	Y	Y	N	Y	*N*
HUMAN HEALTH EFFECTS													
Acute													
Oral LD50	*Y*	*Y*	*Y*	Y	N	Y	Y	N	Y	Y	N	Y	*N*
Inhalation LC50	N			Y	N	Y	Y	N	N	N			N
Dermal LD50	N			Y	N	Y	N			N			N
Skin Irritation	N			Y	Y	Y	Y	N	Y	Y	N	Y	N
Eye Irritation	N			Y	N	N	N			N			N
Repeated dose	*Y*	*Y*	*Y*	Y	U	N	Y	U	Y	Y	N	Y	*N*[b]
Genetic Toxicology – mutation assay	N			Y	Y	N	Y	U	Y	Y	N	Y	N
Genetic Toxicology – chromosomal aberration	*Y*	*Y*	*Y*	N			Y	U	Y	Y	N	Y	*N*
Genetic Toxicology – *in vivo*	N			N			Y	U	N	Y	N	Y	N
Reproductive	*Y*	*Y*	*Y*	Y	N	Y	Y	U	Y	Y	N	Y	*N*[b]
Developmental	*Y*	*Y*	*Y*	N			Y	U	Y	Y	N	Y	*N*[b]

[a] U = unknown
b= OECD 422 proposed
[c] -- means not applicable

REFERENCES

Ashmead, H., D. Graff, and H. Ashmead, 1985. Intestinal absorption of metal ions and chelators. Charles C. Thermon, ed., Chicago, pp. 13-1996. As referenced in Firriolo et al., 1999.

ATSDR, 2001. Draft Toxicological Profile for Cobalt, U.S. Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry (ATSDR), September 2001.

ExxonMobil Chemical Company, 2002. High Production Volume (HPV) Chemical Challenge Program. Test Plan for the Neoacids C5-C28 Category and Robust Summaries for the Neoacids C5-C28 Category. Revised December 19, 2002.

Finlay, C. 2007. Cobalt Borate Neodecanoate Complex: Acute Oral Toxicity Study in Rats - Up-and-Down Procedure Conducted by DuPonts Haskell Laboratories for the Metal Carboxylates Coalition. Study No. 16637

Firriolo, J.M., 1992. Disposition and toxicity after oral and intravenous administration of cobalt naphthenate and cobalt chloride in rats. Ph.D. Dissertation, University of Arizona.

Firriolo, J.M., F. Ayala-Fierro, I.G. Sipes, and D.E. Carter, 1999. Absorption and disposition of cobalt naphthenate in rats after a single oral dose. J. Toxicol. Environ. Health, Part A, 58:383-395.

Glatt, C.A. 2007. Cobalt Borate Neodecanoate Complex: In Vitro Mammalian Chromosome Aberration Test in Chinese Hamster Ovary Cells. Conducted by DuPonts Haskell Laboratories for the Metal Carboxylates Coalition. Study No. 16637

Hoberg, J.R. 2007. Cobalt Borate Neodecanoate Complex - Acute Toxicity to the Freshwater Green Alga, Pseudokirchneriella subcapitata. Conducted by Springborn Smithers Laboratories for the Metal Carboxylates Coalition. Study No. 13865.6106

IUCLID. 2000. Dataset. European Chemicals Bureau, European Commission. Dataset for Neodecanoic Acid, 18 Feb. 2000.

Katz, G.V., and D. Guest, 1994. “Aliphatic Carboxylic Acids,” in Patty’s Industrial Hygiene and Toxicology, 4th ed., Vol. 2, Part E. Clayton, G.D., and F.E. Clayton, eds., John Wiley and Sons.

Lewis J.M., 2007.

Lezotte, F.J. and W.B. Nixon, 2002. Determination of the dissociation constant of prop ionic acid, calcium salt, Wildlife International, Ltd. Study No. 534C-120, conducted for the Metal Carboxylates Coalition.

McLaughlin, S.P. 2007. Cobalt Borate Neodecanoate Complex - Acute Toxicity to the Freshwater Green Alga,Pseudokirchneriella subcapitata. Conducted by Springborn Smithers Laboratories for the Metal Carboxylates Coalition. Study No. 13865.6106

Putt, A.E. 2007. Cobalt Borate Neodecanoate Complex- Acute Toxicity to Water Fleas. Conducted by Springborn Smithers Laboratories for the Metal Carboxylates Coalition. Study No. 13865.6105

Sayers, L.E. 2007. Cobalt Borate Neodecanoate Complex- Acute Toxicity to rainbow trout (*Oncorhynchus mykiss*). Conducted by Springborn Smithers Laboratories for the Metal Carboxylates Coalition. Study No. 13865.6122

Speijers, G.J.A., E.I. Krajnc, J.M. Berkvens, and M.J. van Logten, 1982. Acute oral toxicity of inorganic cobalt compounds in rats. Fd. Chem. Toxic. 20:311-314.

Stopford, W., J. Turner, D. Cappellini, and T. Brock (2003). “Bioaccessibility Testing of Cobalt Compounds.” J. Environ Monit., 5:675-680.

U.S. Environmental Protection Agency, 2002. Draft Action Plan, Development of a Framework for Metals Assessment and Guidance for Characterizing and Ranking Metals. U.S. Environmental Protection Agency, EPA/630/P-02/003A, External Draft Review (June 2002).

U.S. Environmental Protection Agency, 2004. Toxicological Review of Boron and Compounds (CAS No. 7440-42-8) In support of Summary Information on the Integrated Risk Information System (IRIS), EPA 635/04/052.

Woods, W.G., 1994. An introduction to boron: history, sources, uses and chemistry. Environ. Health Perspect. 102(Suppl 7):5-11